Breath Holding Spells; its relation to iron deficiency anemia, and electroencephalogram findings

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Abstract

Background: The objectives of our study were, performing a clinical and laboratory analysis through reviewing the data of 64 child having breath holding spells considering the types of BHS and its relation to iron deficiency anemia ,with special consideration to neurodevelopmental status and EEG finding.

Patients and methods: This study is a prospective hospital based study. It included 64 child with BHS attended Pediatric and Neuropediatric Clinics in both Gannas Medical Center and Saudi- German hospital, Riyadh, Saudia Arabia. Diagnosis of BHS was made clinically by a Pediatrician or a Neurologist based on the history given by the mothers or observation of the spells, detailed clinical data were collected, the needed investigations including, complete blood count (CBC), serum iron, serum ferritin, total iron binding capacity (TIBC), and EEG were done. Patients with hemoglobin level less than 7 gm./dl, a history of febrile convulsions or epilepsy, current treatment with anticonvulsive medications , a clinically identified mental disability, or severe malnutrition were excluded from the study.

Results: 62.5% of children with BHS has anemia, the frequency of BHS has improved markedly with 12 weeks of elemental iron therapy. EEG findings were abnormal in 22 patients with insignificant P value.

Conclusion: We can conclude that, there is a well-known relation between IDA and BHS, there was a higher percentage of consanguinity among the studied children. Elemental iron therapy has an important role in the treatment of BHS through improving the anemia, and so, it should be included in the regular treatment of BHS.

Key words: Breath Holding Spells – Iron Deficiency Anemia

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Introduction

Breath holding spells occur in approximately 5% of the population with equal distribution between males and females. A positive family history can be elicited in 25% of cases. They may be confused with a seizure disorder. Two types of BHS were recognized, cyanotic and pallid BHS [4]. There is a relation between breath-holding spells and anaemia, particularly iron deficiency anaemia. Iron deficiency anaemia may lead to adverse effects on oxygen uptake in the lungs and reduce available oxygen to the tissues, including central nervous system. Despite having many cyanotic attacks per day for several years, the patients do not seem to suffer overt or cumulative brain damage. No specific, long-term psychiatric sequels are detected [1].

Epilepsy is a major differential diagnosis with breath holding spells. The typical full tetrad (provocation by emotion, expiratory apnea and cyanosis, opisthotonic rigidity, and stupor)

readily differentiates breath-holding spells from typical epileptic attacks. The correct diagnosis may require recording a spell by continuous video electroencephalogram (EEG) monitoring [3].

Patients and Methods

This study included 64 child with BHS attended Pediatric and Neuropediatric clinics in both Gannas Medical Center and Saudi- German Hospital, Riyadh, Saudia Arabia. Age range was from 4 months to 4 years, 59%e males. Diagnosis of BHS was made clinically by a Pediatrician or a Neurologist based on the history given by the mothers or observation of the spells, detailed clinical data were collected, the needed investigations were done including complete blood count (CBC), serum iron, serum ferritin, total iron binding capacity (TIBC), and electroencephalogram (EEG). Forty patients out of the sixty four patients with BHS were have iron deficiency anemia, those anemic patients were treated with elemental iron (6mg/kg/day) for 12 weeks. Patients with hemoglobin level less than 7 gm./dl, a history of febrile convulsions or epilepsy, current treatment with anticonvulsive medications , a clinically identified mental disability, or severe malnutrition were excluded from the study. Clinical, laboratory, and EEG data were entered into the SPSS 10 (Statistical Package for the Social Science; SPSS Inc., Illinois, USA) for descriptive statistics.

Results

62.5% of children with BHS has anemia, the frequency of BHS has improved markedly with 12 weeks of elemental iron therapy. EEG findings were abnormal in 22 patients with

insignificant P value. Detailed results are explained in the following tables at the end of the article.

Table (1): Patients characteristics in studied children

Characteristics		Summary statistics
Type of spells	Cyanotic	46 (71.88%)
	Pallid	18 (28.12%)
Provoking factors	Crying	54 (84.38%)
	Anger & crying	8 (12.50%)
	Anger	2 (3.13%)
Convulsions	No	48 (75.00%)
	Yes	16 (25.00%)
Consanguinity	No	30 (46.88%)
	Yes	34 (53.13%)
Family History	No	44 (68.75%)
	Yes	20 (31.25%)

Table (2): Improvement of anemia with 8 weeks elemental iron treatment

	Total number of anemic cases with BHS = 40 cases		
Severity of anemia (hemoglobin level)	Less than 8gm/dl	8-10 gm/dl	More than 10gm/dl
Baseline	2 (5%)	22 (55%)	16 (40%)
At 4 weeks treatment	1 (2.5%)	9 (22.5%)	30 (75%)
At 8 weeks treatment	0	2 (5%)	38 (95%)

P value < 0.001

Table (3): Frequency of BHS and its improvement with iron therapy

	Number of spells /week		
	< 5	5 – 10	>10
Baseline	3 (7.5%)	30 (75%)	7 (17.5%)
At 4 weeks treatment	14 (35%)	21 (53%)	5 (12%)
At 8 weeks treatment	34 (85%)	6 (15%)	0

P value < 0.001

Table (4): EEG of the studied children

Characteristics	**Summary statistics**	**Kind of anemia**		
EEG		IDA	NON IDA	P value
Normal	42 (65.63%)	30	12	0.25
Abnormal	22 (34.37%)	10	12	
Kind of EEG waves				
Focal epileptic discharge	20 (31.25%)			
Generalized cerebral dysrhythemia	2 (3.12%)			

Discussion

Breath-holding spells occur in 5% of otherwise healthy children .Breath holding spells can be dramatic and recurrent alarming episodes. Most pediatricians have offered parents the reassurance that these alarming episodes are not life threatening and are likely to resolve spontaneously with time [17].

Concerning the type of BHS in our study (table 1), cyanotic BHS were detected in 71.88%, these results were in agreement with that of Ashrafi (79%) and Paul SM (60%) [3 , 14], but were lower than that of Anil BG (94%) [2]. Bhat MA studied 59 cases of which 63% had cyanotic spells only, 12% had pallid spells, and 25% had both types with one predominating over the other [5]. Pallid BHS result from exaggerated, vagally-mediated cardiac inhibition, whereas the more common , cyanotic BHS are of complex pathogenesis which is not completely understood [9].

Provoking factor was noticed in all patients . In our study (table1), crying is the commonest triggering factor (84.38%). In other studies, Anger and frustration were the common triggering factors in 90.0% of cases [6]. In Ashrafi's study anger and pain were the common triggering factors (65.1%) [3].

Convulsions were associated with BHS in 25% of our studied children (table1), results lower than that of Bhatia MS (84.00%) [6]. The convulsive movements seen during BHS are reflex anoxic seizures, which are not epileptic and do not require antiepileptic medication. Probably these patients have a lower seizure threshold and hypoxia-ischemia that triggers the seizures [8]

Consanguinity was present in 53.13% of our patients (table1), results much higher than that of Ashrafi's study (30%) [3], and that of Hilal M (8.7%) [10], this can be explained by the

fact that relatives marriage traditionally present in high ranges in Saudia Arabia where our study was done.

Concerning family history, Positive family history was present in 31.25% of our patients (table1), result in agreement with that of Paul SM (35%), Zehetner AA (30%) [14, 16], but lower than that of Ashrafi's study (51.2%) [3] and that of Daoud AS (47.5%) [7].

In our study, iron deficiency anemia was observed in 62.5% of the studied children with BHS. Results in agreement with that of Tonekaboni (68.6%) [15]. Mechanism of link between BHS and IDA is not clear. It has been postulated that decrease oxygen concentration in the lung and in the brain in IDA causes BHS [6]. It has been proposed that iron plays an important role in regulation of the neurologic function, it may reduce the monoamine oxidase in the brain by increasing the urinary norepinephrine and since this enzyme regulate many brain activities, its deficiency may have adverse effect on the brain function {16}. These results were slightly higher than that of Ashrafi (53%) [3]and that of Handan G (56%) [11]. This can be explained by bad nutritional habits specially at time of weaning and lack of iron supplements. But results were lower than that of Hilal M (69.2%) [10]. This can be explained by the marked improvement of formula production which is the predominant form of feeding in the early life in Saudia Arabia. Most types of formula became enriched with iron and other vitamins. As reported previously, a low serum ferritin may be the earliest laboratory finding of IDA [7].

Our study (Table 2) showed an improvement in the hemoglobin level with 12 weeks of iron therapy with a statistically significant value (P value < 0.001). Several studies have reported abatement of BHS with iron treatment, which may suggest a relation between IDA and BHS [6 , 7], however , iron deficiency is not the only factor responsible for BHS because not all children with BHS were iron deficient at baseline [10]. Daoud demonstrated that iron

treatment is effective in treatment of BHS and that iron deficient children are more likely to benefit from such treatment [7]. It is not known exactly how iron deficiency causes BHS but it has been proposed that iron plays a role in catecholamine metabolism and neurotransmitters in the central nervous system [13].

Our study (Table 3) showed a statistically significant decrease (P value < 0.001) in the frequency of BHS with 8 weeks of iron therapy . Ziaullah Showed a significant decrease in the severity and frequency of BHS with oral iron therapy [17].. Mocan H evaluated the prognosis of BHS after iron treatment, significant difference in the frequency of cyanotic spells between children who had received iron and those who had not (84% v 21.4%). They suggested that iron may be crucial in the treatment of BHS because iron deficiency may be the main underlying defect [10].

Concerning EEG findings (Table 4), EEG was normal in 65.63% of the studied patients and abnormal in 34.37%, no significant statistical difference was found. Abnormalities detected were focal mild epileptic discharge in 20 patients (31.25%), and generalized cerebral dysrhythemia in two patients (3.12%). In study by Hallioglu (37.5%) showed epileptogenic EEG abnormalities, (12.5%) showed benign EEG variants and (50%) showed completely normal EEG recording. Focal epileptiform discharge detected in the patients originated from centrotemporal and centroparietal regions. In Hilal M study, abnormal EEG detected in 20% of the studied patients in the form of slight or moderate EEG abnormalities [13]. In the study done by Ashrafi, all of the patients had normal EEG recording [3].

The limitation of our study relies on the reduced number of the available cases and the incompliance of the studied children and their families to the requested investigations and EEG.

Conclusion

We can conclude from our study that, there is a well-known relation between IDA and BHS. Elemental iron therapy has an important role in the treatment of BHS through improving the anemia, it should be included in the regular treatment of BHS.

Author's contribution

1. Mostafa M Abosdera: History taking, clinical examination, and requesting the needed investigations for the studied children, analyzing the collected data, collecting the scientific materials, writing and revising the manuscript.
2. Mahmoud M Sabry: Neurological examination of the studied children, helping in collection of the scientific materials, and analyzing the EEG findings.
3. Ehab S Abdel-Moneim: Collection of scientific materials, writing and revising the manuscript, and statistical analysis of the study.

Conflict of interests

The authors declare that they have no financial or nonfinancial conflicts of interests related to the subject matter or materials discussed in the manuscript.

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